REMARKS

Following entry of the present amendment, claims 1, 3-10, 12-16, 21, 22, 26, 27, 29-32, 50-87, 89-97, and 101-119 will be pending in the present application. Claim 2 has been cancelled and claims 1, 21, 30, 56, 59, 71, 89, and 94 have been amended by the above amendments. Claim 1 has been amended to exclude "non-hygroscopic excipients" from the claim. Claims 56, 71, and 89 have been amended to remove "bile salt derivative" embodiments. Claims 21, 30, 59, and 94 have been amended to fix typographical errors. No new matter has been added.

Attached is a marked-up version of the changes being made by the current amendment.

The Office Action mailed June 12, 2002 reiterates that claims 1, 3-10, 12-16, 31, 101, 102, and 103-118 are characterized as allowable to the extent they have been examined, as set forth in the Office Action mailed December 28, 2001. Applicants again bring to the Examiner's attention claim 119, added with the amendment filed on October 4, 2001, which was not addressed by the present nor the previous Office Action. As it depends from allowable claim 102, acknowledgement that claim 119 is also allowable is respectfully requested.

In the telephonic interview with the undersigned on February 7, 2002, the Examiner indicated that claim 1 would be allowable if part (C) were deleted from the claim or amended to exclude the possibility that the "additive" is an active ingredient that does not meet the diameter limitation applied to parts (A) and (B). In the Response to Office Action filed April 9, 2002, Applicants amended claim 1 to exclude this possibility by replacing the term "additive" with "excipient." In the current Office Action, the Examiner has deemed this amendment non-responsive. According to the Examiner, the term "excipient" is "very much imprecise, and is not effective to exclude any and all biologically active peptides." Accordingly, the Examiner asserted that the amendment to claim 1 has not brought the claims into compliance with the restriction requirement mailed December 30, 1999.

Applicants respectfully disagree with the Examiner that the term "excipient" is "very much imprecise" as to biological activity. As discussed in the Response filed April 9, 2002, "excipients" are, by definition, inert substances. However, in an effort to advance prosecution,

Applicants have amended claim 1 to delete part (C), as suggested by the Examiner during the telephonic interview. Thus, allowance of claim 1 is requested. Applicants maintain the right to file a divisional application to cover the embodiments so excluded.

The Examiner indicated that the method and apparatus claims can be rejoined with the composition claims if they were amended to have the same scope as the allowed composition claims. The Examiner asserted that because "bile salt derivative" was not within the scope of claim 1, claim 56 would not be rejoined in its present form. To comply with the restriction requirement, Applicants have amended claims 56, 71, and 89 to remove "bile salt derivative" from the list of surfactant compound embodiments. Thus, rejoinder and allowance of claims 21, 22, 26, 27, 29, 30, 32, 50-87, and 89-97 is respectfully requested.

Claims 30, 59, and 94 have been amended to change "surfacant" to "surfactant," thereby correcting an inadvertent typographical error. Claim 21 has been amended to correct the inadvertent omission of "the" before "composition of claim 1." Applicants apologize for these errors.

In reviewing references cited in related applications, Applicants noted that some were not of record in the present case. These references are included in the enclosed Information Disclosure Statement. The Examiner is respectfully requested to initial the Form 1449 and return it to Applicants.

In addition, Applicants have not yet received an initialled Form 1449 for the Information Disclosure Statements filed on August 20, 1999, and April 9, 2002. The Examiner is respectfully requested to initial all references cited therein and return the forms to Applicants.

Applicants bring to the Examiner's attention the following applications and patents, all of which are related to the present application and assigned of record to the assignee of the present application:

U.S. Patent No. 5,506,203

U.S. Patent No. 5,518,998

U.S. Patent No. 5,658,878

U.S. Patent No. 5,747,445

U.S. Patent No. 5,830,853

U.S. Patent No. 5,952,008

U.S. Patent No. 6,004,574

U.S. Patent No. 6,165,976

U.S. Patent No. 6,306,440

U.S. Reexamination Certificate No. 5,506,203 C1

U.S. Reexamination Certificate No. 5,518,998 C1

U.S. Application Serial No. 08/960,093

U.S. Application Serial No. 09/158,554

U.S. Application Serial No. 09/383,590

U.S. Application Serial No. 09/665,585

U.S. Application Serial No. 09/731,429

U.S. Application Serial No. 09/783,189

Applicants ask that all claims be allowed. Please apply any charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

Date: July 12, 2002

Janis K. Fraser, Ph.D., J.D.
Reg. No. 34,819

Fish & Richardson P.C.
225 Franklin Street
Boston, Massachusetts 02110-2804
Telephone: (617) 542-5070
Facsimile: (617) 542-8906

Version with markings to show changes made

In the claims:

Claim 2 has been cancelled.

Claims 1, 21, 30, 56, 59, 71, 89, and 94 have been amended as follows:

1. (Four Times Amended) A propellant-free composition consisting of (A) a polypeptide, and (B) one or more surfactant compounds which (i) have a consistency that permits them to be processed into primary particles having a diameter less than 10 microns, and (ii) enhance the systemic absorption of said polypeptide in the lower respiratory tract of a patient, [and (C) optionally one or more non-hygroscopic excipients,] said composition being in the form of a dry powder suitable for inhalation from a dry powder inhaler device, wherein at least 50% of the total mass of (A) and (B) consists of primary particles having a diameter less than 10 microns or equal to about 10 microns, and wherein each of the one or more surfactant compounds is selected from the group consisting of a salt of a fatty acid, bile salt, single-chain phospholipid, double-chain phospholipid in which each chain of the double-chain phospholipid is eight or fewer carbon atoms in length, alkyl glycoside, cyclodextrin or derivative thereof, salt of a glycyrrhizine acid, salt of a saponin glycoside, salt of an acyl carnitine, and sodium salicylate.

21. (Thrice Amended) A method for systemic administration of a biologically active polypeptide, comprising

providing the composition of claim 1; and

causing said patient to inhale said composition from a dry powder inhaler device.

30. (Twice Amended) The method of claim 29 wherein the surfactant [surfacant] compound is sodium caprate.

56. (Twice Amended) The method of claim 21, wherein said surfactant compound is [a bile salt derivative,] an alkyl glycoside, a cyclodextrin or derivative thereof, or a phospholipid.

59. (Twice Amended) The method of claim 21, wherein said surfactant [surfacant] compound is a bile salt.

71. (Amended) The composition of claim 70, wherein said surfactant is a bile salt, [a bile salt derivative,] an alkyl glycoside, a cyclodextrin or derivative thereof, or a phospholipid.

89. (Twice Amended) The dry powder inhaler device of claim 78, wherein said surfactant compound is [a bile salt derivative,] an alkyl glycoside, a cyclodextrin or derivative thereof, or a phospholipid.

94. (Twice Amended) The dry powder inhaler device of claim 78, wherein said surfactant [surfacant] compound is a bile salt.